

The importance of matrix metalloproteases in the pathology of the tempo-mandibular joint in children

Gaffarov S.A.¹, Saidov A.A.²

¹*Tashkent Institute of Advanced Medical, Tashkent city, Uzbekistan*

²*Bukhara State Medical Institute, Bukhara, Uzbekistan*

Email: gaaffarov_s@umail.uz

ABSTRACT

Among the reasons for patients visiting a dentist, one of the most common is the pathology of the temporomandibular joint (TMJ), which occurs in 25-50% of the population [2,3,4]. According to the classification of ICD-10, TMJ diseases are classified as class XII " Maxillofacial abnormalities (including malocclusion) "and Section 6" Temporomandibular joint diseases ", arthropathy and arthrosis of all joints of various etiologies are also described in class XIII" Diseases of the musculoskeletal system and connective tissue ". TMJ internal disorders are referred to in this classification by the terms "clicking jaw", "TMJ dislocation and subluxation".

Keywords: Maxillofacial anomalies, diseases of the temporomandibular joint.

1. RELEVANCE

Osteoarthritis of the temporomandibular joints occurs in 76.8% of patients with dentoalveolar anomalies and muscular-articular dysfunctions [7.8]. In the literature available to us, unfortunately, there is no consensus on the prevalence of internal disorders in TMJ in children, this question is currently time remains debatable.

A number of authors suggest that connective tissue dysplasia, which is often manifested by pathology of the musculoskeletal and ligamentous apparatus, is one of the factors in the development of internal disorders in the temporomandibular joint [1,4,5,6]. As a result of the research, Kupriyanov I.A. et al. (2003), Ivasenko P.I. et al. (2007) found that in patients with connective tissue dysplasia and internal disorders of the temporomandibular joint, catabolic processes prevail in the tissues, chronic inflammation with a pronounced productive component, manifested by edema of the connective tissue, perivascular infiltrates, homogenization of collagen fibers, hyalinosis, expressed sclerosis, is diagnosed. which causes a more severe course of the disease due to obliteration of blood vessels, deterioration of trophism of the capsular-ligamentous apparatus. The consequence is a more dynamic development of the pathological process, the occurrence of such complications as osteoarthritis, synovitis, the rapid appearance of irreversible deformations in the temporomandibular joint [I. Kupriyanov et al., 2003; Ivasenko P.I. et al., 2007]. With the pathology of TMJ, the cartilage metabolism is disturbed, the activity of the enzymes involved in the breakdown of aggrecan changes. A number of authors determined the molecular forms of the matrix of metalloproteinases (MMPs), including collagenases (MMP-1, MMP-8 and MMP-13) and (MMP-2 and MMP-9), in synovial fluid in patients with internal disorders of the temporomandibular joint of the lung and moderate severity. As a result of the studies, it was found that elevated levels of MMP-2, MMP-9 and MMP-8 in the synovial fluid of patients with TMJ pathology reflect the destruction of collagen of the Type into the active phase of the destruction of the temporomandibular joint elements, which can be used for diagnostic purposes [9 , 10,11,].

According to modern concepts, the pathogenesis of TMJ dysfunction consists of sequential events starting with the development of occlusal disorders, stress, leading to spasm of the masticatory muscles, manifested by muscle pain, displacement and restriction of the movements of the lower jaw, which, in turn, disrupts dynamic occlusion, in the future internal disturbances occur, manifested by clicking, which is replaced by intermittent blocking in the joint of a displaced disk and ends with the development of

destructive changes in tnyh structures, ie osteoarthritis [8.12]. In the literature available to us, there is currently no consensus on the etiology and pathogenesis of internal disorders in the temporomandibular joint in patients of different ages. This issue is currently under discussion and needs further study.

2. MATERIAL AND RESEARCH METHODS

Examination of sick children included a survey, examination, assessment of the state of hard tissues of teeth, noted the presence of abnormalities and deformations of the dentition, the condition of the temporomandibular joint. When collecting an anamnesis, complaints were clarified when pain or noise in the temporomandibular joint first appeared, how often they occur, whether treatment was carried out, how effective it was.

An examination of the oral cavity was carried out in a dental office, with artificial lighting using a standard set of dental instruments - a mirror and a dental probe. Data on the displacement of the lower jaw in the vertical, sagittal and transversal planes were obtained during external examination of the face with closed dentition in the position of relative physiological rest and with maximum opening of the mouth. Patients were examined according to a single protocol, which included: determining the type of bite, KPI index, the ratio of the first permanent molars according to Engle's classification, KPU index, IROPZ index of 1 and 2 molars according to V.Yu. Milikevich, 1984. Palpation of the temporomandibular the joints were passed through the skin, in front of the tragus of the ear or through the front wall of the external auditory canal when the lower jaw was closed and with its movements. Palpating the masticatory muscles, painful and compacted areas, the presence of trigger points were determined. The degree of dysfunction of the temporomandibular joint was determined using the Helkimo clinical index. Questioning of the subjects was carried out using a specially designed questionnaire to identify TMJ pathology, the assessment was carried out in points. An X-ray examination of the temporomandibular joint in 45 sick children aged 6 to 15 years with internal disorders of the temporomandibular joint was carried out in Bukhara. The results of a dental examination of patients were entered on the outpatient's medical card F-043 / u-2/88, for students of schools - in the rehabilitation card (registration form 267) and a specially designed card for assessing dental status. In the passport part of the card, the identification number, last name, first name, middle name, year of birth, date of filling, address, transferred and associated diseases were recorded. The content of MMP-1, MMP-9, TIMP-1 in blood serum was determined by enzyme-linked immunosorbent assay using standard test kits ("HUMAN", Germany) in accordance with the attached instructions. The control group consisted of 15 healthy children without signs of TMJ.

Statistical processing of the obtained data was performed using the SPSSStatistics 21.0 program. Differences were considered statistically significant at $p < 0.05$.

3. RESEARCH RESULTS AND DISCUSSION

In our study, the choice of MMP-1, which is interstitial collagenase and MMP-9, acting on the collagen of the basement membranes, was carried out taking into account the fact that the extracellular matrix and basement membrane have a different structure and composition, and TIMP-1 is able to inhibit both of these proteinases.

In 45 examined children with TMJ, serum matrix metalloproteinases of types 1 and 9 (MMP-1 and MMP-9) were studied, which play a central role in the metabolism of connective tissue proteins and are specific markers of collagen breakdown (Gasanov A.G., 2010) . The biochemical parameters of blood serum in children with TMJ are presented in table 1. A significant increase in the content of MMP-1 in children with TMJ was noted as the main enzyme that denatures fibrillar collagen of the extracellular matrix. Similar changes were revealed in the study of the content of MMP-9, the concentration of which in children of the main group was 1.6 times higher than in children of the comparison group, which, according to N.I. Solovieva and O.S. Ryzhakova (2010), may indicate the activation of type IV collagen hydrolysis. The concentration of TIMP-1 in cases of TMJ has decreased when compared with a control group of children. The increased coefficients MMP-1 / T1MP-1 and MMP-9 / TIMP-1 confirm the possibility of exceeding the rate of collagen degradation by matrix proteinases at the rate of its synthesis.

Table 1. Comparative characteristics of the content of matrix metalloproteinases in blood serum in children with TMJ, $M \pm m$

Indicator	Survey groups	
	Children with TMJ, $n = 45$	Healthy children (control) $n = 15$
ММР-9, нг/мл	$118,17 \pm 8,63^*$	$73,97 \pm 5,19$
ММР-1, нг/мл	$11,11 \pm 1,08^*$	$4,37 \pm 0,53$
ММР-3, нг/мл	$38,04 \pm 3,14^*$	$7,72 \pm 0,61$
<i>TIMP-1</i> , нг/мл	$598,62 \pm 18,91$	$728,32 \pm 19,13$
<i>MMP-1/TIMP-1</i> , усл. ед	0,003	0,002
<i>MMP-9/TIMP-1</i> , усл. ед.	1,33*	0,54

Note: * - significance of differences $P < 0.05$ with respect to control data

Representatives of the MMP groups are also interstitial collagenase MMP-3, which break down the fibrillar collagen of the corresponding types, as well as naproteoglycans, laminin, fibronectin and amorphous collagen. In our studies, presented in table 1, a significant increase in MMP -3 was indicated in children with TMJ pathology, as compared with healthy children.

The revealed imbalance of type I and type III collagens due to the high activity of metalloproteases with PG indicates a predominance of synthesis of type III collagen, which relates to embryonic proteins with low strength, which correlates with a systemic decrease in the level of collagen that determines the integrity of connective tissue in the dentofacial system. Decreased synthesis of total collagen and the predominance of its immature fraction with a deficiency of components of the intracellular matrix, which determine the weakening and overstretching of connective tissue. The differences in the number, nature of the distribution and localization of collagen and elastic fibers along with impaired expression of protein-coding genes, in particular, the MMP and TIMP families, determine the multilevel changes in the microarchitectonics of the dentofacial system in children with TMJ.

Thus, in children with TMJ, there is a change in the activity of type 1, 3, 9 matrix metalloproteinases in the blood serum, indicating remodeling of connective tissue, indicating metabolic disturbances.

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